REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

I. Status of the Claims

Claims 2-6, 9, 10, 14, 15, 20-33, 35, 36, 38-44, 48 and 49 were cancelled previously.

Claim 1 is amended to recite an "injectable formulation comprising a single pharmaceutical composition." Claims 34 and 45-47 are likewise amended to recite a "single product" comprising first and second pharmaceutical compositions. Support for the claim amendments may be found in the specification, including at paragraphs [0017] and [0059] to [0071].

Claims 50 and 51 are added to recite specific embodiments. Claim 50 recites a product comprising one or more unit doses of an injectable formulation, in which the injectable formulation is as recited in claim 1. Claim 50 is supported by claim 1 (the injectable formulation); paragraph [0053] (the product can contain a combination of both FSH and hCG, "injectable formulations may be supplied as a product having pharmaceutical compositions"); paragraph [0055] (compositions supplied in dosage unit form); and paragraph [0056] (specific unit dosage forms). Claim 51 depends from claim 50 and recites a product supplied in a pre-filled syringe or cartridge. Claim 51 therefore parallels claim 18 and is further supported by paragraph [0053] in the specification.

None of the foregoing amendments introduce new matter. The foregoing amendments are made without prejudice or disclaimer, solely to advance prosecution, and not in acquiescence to any rejection. The right to pursue any cancelled subject matter in a continuing application is expressly reserved.

Following entry of these amendments, claims 1, 7, 8, 11-13, 16-19, 34, 36, 37, 45-47, 50 and 51 will be pending, of which claims 1, 34, 45-47, and 50 are independent. These claims are presented for reconsideration.

II. Non-Finality Of the Previous Office Action

Applicant notes the indication at page 2 of the Action that the previous Office Action "inadvertently" indicated that the action was a "final" Action, although it was "intended to be a non-final action." Although Applicant appreciates the Examiner's apology, Applicant notes that it proceeded with the understanding that the action was "final," and so restricted the claim amendments to those that should be acceptable after final, and did not submit an IDS to cite the newly issued Office Actions from the co-pending applications. Thus, Applicant was indeed restrained by the improper "final" indication. Now that this Action is again a "final" one, Applicant is filing an RCE to ensure that the next Action will be non-final.

III. Information Disclosure Statement

The Office Action notes that only Office Actions from co-pending applications that are listed on a 1449 (SB08) will be considered. As explained above, Applicant did not submit the Office Actions from the co-pending application with the previous response because Applicant understood that the previous Office Action was "final." The Examiner did not correct this error until the current, final Office Action was issued. Thus, Applicant never had an opportunity to submit the Office Actions. Now that Applicant has filed an RCE, Applicant submits herewith an IDS to make of record the Office Actions that the Examiner has issued in the co-pending applications. Thus, consideration thereof is respectfully requested.

IV. Rejections under 35 U.S.C. § 102

A. The Rejections

At pages 4-7, the Examiner maintains the following 35 U.S.C. § 102(b) rejections of :

(a) claims 1, 11-13, and 19 over Filicori *et al.*, "Low-dose human chorionic gonadotropin therapy can improve sensitivity to exogenous follicle-stimulating hormone in patients with secondary amenorrhea," *Fertility and Sterility* 72 (6): 1118-1120 (1999) ("Filicori");

(b) claims 1, 11, 13, 16, and 19 over Thompson *et al.*, "Gonadotropin requirements of the developing follicle," *Fertility and Sterility* 63 (2): 273-276 (1995) ("Thompson");

(c) claims 1, 7, 8, 11, 13, 16, and 19 over Menezo, WO 03/022303 ("Menezo"); and

(d) claim 45 over Skrabanja *et al.* U.S. Patent No. 5,929,028 ("Skrabanja").

At page 11, claims 34, 47 and 46 are newly rejected under 35 U.S.C. § 102(e) over Sharma *et al.*, U.S. Patent Application Publication No. 2003/0181361 ("Sharma").

Applicant respectfully traverses these rejections.

B. The Claimed Invention

As taught in the specification, Applicant has found that the combination of a specific amounts of FSH and specific amounts of hCG are particularly effective for treating infertility, such as by showing improved ovulation and pregnancy rates. Specification, paragraphs [0060] to [0074], and Table 1. Claims 1, 7, 8, 11-13, and 16-19 recite injectable formulations comprising a single pharmaceutical composition consisting essentially of FSH and hCG in a pharmaceutically acceptable carrier, having specific amounts of FSH and hCG. Claims 34, 37, 45, 46 and 47 recite products comprising a first pharmaceutical composition comprising recombinant FSH and a second pharmaceutical composition comprising recombinant hCG, wherein the compositions have recited amounts of recombinant FSH and/or recombinant hCG. Such formulations and products are not taught or suggest by the cited references.

C. Filicori

The Examiner alleges that Applicant's previous arguments regarding Filicori's failure to teach a single composition comprising both FSH and hCG are not persuasive, because "claim 1 does not recite 'single vial' or 'single syringe,'" or otherwise recite that the recited formulation is a single composition. Office Action at page 5. Without acquiescing to the corrections of the Examiner's claim construction, and solely to advance prosecution, Applicant has amended claim 1 to expressly recite a "single" composition.

Claim 1, therefore, recites injectable formulations comprising a ***single composition*** consisting essentially of specific amounts of FSH ***and*** hCG, in a pharmaceutically acceptable carrier. Because Filicori does not teach or suggest such a composition, claim 1, and

dependent claims 11-13, 16 and 19, are not anticipated by Filicori. Thus, Applicant respectfully urges reconsideration and withdrawal of this rejection.

D. Thompson

At pages 5-6 of the Office Action, the Examiner states that the rejection of claims 1, 11, 13, 16 and 19 over Thompson is maintained "for the reasons discussed above in the maintained rejection [over Filicori]." Office Action at page 6. Applicant understands this to mean that the rejection is maintained because the claims do not explicitly recite a "single" composition. As noted above, claim 1 is amended to recite a "single" composition. Thus, it is believed that this rejection, like the rejection based on Filicori, is overcome. As noted previously, Thompson does not teach a ***single composition*** with ***both*** FSH and hCG. For example, at page 274, col. 2, Thompson distinguishes between "IM" (intramuscular) administration of FSH and "SC" (subcutaneous) administration of hCG. Clearly, this requires the use of separate compositions suitable for different routes of administration, and administered separately. Applicant therefore respectfully urges reconsideration and withdrawal of this rejection.

E. Menezo

At page 6 of the Office Action, the Examiner states that the rejection of claims 1, 7, 8, 11, 13, 16, and 19 over Menezo is is maintained "for the reasons discussed above in the maintained rejections [over Filicori and Thompson]." *Id.* Again, Applicant understands this to mean that the rejection is maintained because the claims do not explicitly recite a "single" composition, and again, Applicant believes that this rejection is obviated by the amendments to claim 1. Like Filicori and Thompson, Menezo does not disclose a ***single pharmaceutical composition*** with ***both*** FSH and hCG. Quite to the contrary, Menezo teaches that FSH and hCG are administered at different time points (often indeed on different days), and according to different administration regimes, and so would not be combined together. Thus, Applicant respectfully urges reconsideration and withdrawal of this rejection.

F. Skrabanja

At page 7 of the Office Action, the Examiner states that the rejection of claim 45 over Skrabanja is maintained "for the reasons discussed above in the maintained rejections [over Filicori, Thompson, and Menezo]." *Id.* Applicant understands this to mean that the rejection is maintained because the claims do not explicitly recite a "single" product comprising the recited first and second compositions. The Office Action also cites Skrabanja's teaching that formulations may comprise FSH or hCG or mixtures thereof, and its general teachings that FSH compositions may comprise from 2-200 ug/mL FSH. Applicant respectfully traverses this rejection.

Claim 45 is directed to a single product comprising (i) a first pharmaceutical composition comprising recombinant FSH and (ii) a second pharmaceutical composition comprising recombinant hCG, wherein the amount of recombinant hCG in the second pharmaceutical composition is about 0.1 μg to about 2,000 mg/ml. Skrabanja does not teach or suggest such a product.

Skrabanja is directed to stable formulations of known active ingredients, and methods of making them. While Skrabanja teaches compositions that comprise FSH or hCG or both "in admixture", Skrabanja does not teach or suggest a ***single product*** that comprises ***two separate compositions***, one comprising recombinant FSH and the other comprising recombinant hCG. Applicant emphasizes that, although Skrabanja mentions that FSH and hCG can be "dissolved together," Skrabanja, column 6, lines 42 to 46, this teaching does not relate to the single. multi-component product recited in claim 45.

Accordingly, Skrabanja does not anticipate claim 45, and Applicant respectfully urges reconsideration and withdrawal of this rejection.

G. Sharma

At page 11, claims 34, 46 and 47 are newly rejected under 35 U.S.C. § 102(e) over Sharma. Applicant respectfully traverses.

Claim 34 is directed to a single product comprising (i) a first pharmaceutical composition comprising recombinant FSH and (ii) a second pharmaceutical composition comprising recombinant hCG, wherein the amount of recombinant hCG in the second pharmaceutical composition is selected from the group consisting of 1, 2, 3, 4 or 8 μg hCG.

Claim 46 is directed to a single product comprising (i) a first pharmaceutical composition comprising recombinant FSH and (ii) a second pharmaceutical composition comprising recombinant hCG, wherein the amount of recombinant hCG in the second pharmaceutical composition is about 0.1 μg to about 2,000 mg/ml.

Claim 47 is directed to a single product comprising (i) a first pharmaceutical composition comprising recombinant FSH and a second pharmaceutical composition comprising recombinant hCG, wherein the amount of recombinant FSH in the first pharmaceutical composition is from about 0.1 μg to about 2,000 mg/ml and the amount of recombinant hCG in the second pharmaceutical composition is about 0.1 μg to about 2,000 mg/ml.

Sharma does not teach or suggest such products. As noted in the Office Action, Sharma is directed to extended release formulations of recombinant proteins. Sharma focuses on erythropoietin, but also lists many possible recombinant proteins to be formulated in accordance with its technology. Sharma's broad disclosure of numerous possible recombinant proteins would not have led the skilled artisan to compositions comprising the specific proteins recited in the claims, in the amounts recited in the claims. Moreover, Sharma does not provide any teaching, suggestion or reason to prepare or provide a ***single product*** comprising ***both*** (i) an FSH composition and (ii) an hCG composition. Thus, the anticipation rejection based on Sharma is improper, and should be withdrawn.

H. Claims 50 & 51 Are Not Anticipated

New claims 50 and 51 are not anticipated by any of Filicori, Thompson, Menezo or Skrabanja. These claims are directed to a single product comprising one or more unit doses of an injectable formulation comprising a single pharmaceutical composition consisting essentially of FSH and hCG in at least one pharmaceutically acceptable carrier, where the

single composition contains specific amounts of FSH and hCG. As none of Filicori, Thompson, or Menezo teach or suggest a single composition with both FSH and hCG, these refernece cannot anticipate claims 50 and 51. Moreover, as Skrabanja does not teach or suggest a composition comprising the specifically recited amounts of FSH and hCG, Skrabanja likewise cannot anticipate claims 50 and 51. Thus, these claims should be found to be free of the prior art.

V. Rejection under 35 U.S.C. § 103

A. The Rejections

The Office Action maintains and/or makes the following 35 U.S.C. § 103 rejections:

(a) claims 17 and 18, as allegedly obvious over Menezo and Skrabanja; and

(b) claim 37, as allegedly obvious over Sharma and Skrabanja.

Applicant respectfully traverses these rejections.

B. Claims 17 and 18 in view of Menezo and Skrabanja

At pages 7-9 of the Office Action, the Examiner has maintained the rejection of claims 17 and 18 as allegedly rendered obvious by the combination of Menezo and Skrabanja. In maintaining the rejection the Examiner states that "the instant claims do not recite 'single vial combinations of FSH and hCG' or 'single syringe combinations of FSH and hCG." Office Action at page 9. As discussed above, claim 1, from which claims 17 and 18 depend, is amended to recite a "single" composition. Thus, this basis for maintaining the obviousness rejection has been removed.

As shown above, Menezo does not disclose or suggest an injectable formulation comprising a ***single*** pharmaceutical composition with ***both*** FSH and hCG, let alone a single composition comprising FSH and hCG in the very specific amounts recited in claim 1. Indeed, Menezo describes administering FSH and hCG at different time points, often on different days, and according to different administration regimes, thereby requiring separate compositions. For example, the kits defined in claim 31 of Menezo include separate and different doses of FSH and hCG and different numbers of doses of FSH and hCG. Menezo

reveals no contemplation that FSH and hCG should be administered in the same preparation and, to the contrary, teaches away from that aspect of the present invention by teaching administration schedules that require the FSH and hCG to be provided and administered separately.

Skrabanja is cited for teaching liquid forms of FSH and hCG, various doses of FSH and hCG, and a combination of FSH and hCG dissolved together. Office Action, page 9. However, Skrabanja does not teach or suggest a composition with the very specific amounts of FSH and hCG recited in the rejected claims. Skrabanja only discloses broad ranges of possible doses of each hormone, without any guidance that would lead the skilled artisan to the recited amounts. Skrabanja does not even suggest the recited doses of one or the other of FSH and hCG, let alone the specific recited dosage combinations. Skrabanja's broad teaching is insufficient to establish obviousness of the specific amounts recited in the instant claims. *See* MPEP § 2144.08.

Moreover, the rejection is just the type of impermissible hindsight rejection criticized in *In re Kubin*, 561 F.3d 1351, 1359 (Fed. Cir. 2009), where the court explained that merely throwing "metaphorical darts at a board filled with . . . prior art possibilities" does not give rise to obviousness. Here, there is a nearly infinite number of possible combinations of dosages within the broad teachings of Skrabanja, and no guidance or "bull's eye" to lead to the present invention.

Combining Menezo with Skrabanja does not strengthen the obviousness rejection, as the skilled artisan reading both references still would not be led to the present invention. Although Skrabanja indicates that FSH and hCG can be provided in a single composition, Menezo provides no reason for making a single preparation comprising both FSH and hCG in the same composition, let alone in the recited amounts. To the contrary, as discussed above, Menezo discloses specific dosing regimens wherein FSH and hCG must be administered at different times, including at different times that are several days apart. Thus, even the skilled artisan aware of both Menezo and Skrabanja would not have a reason to make a composition as claimed, because they would not find any reason in these references to prepare a single composition comprising FSH and hCG in the specific amounts recited in the claims.

Although *KSR* may have broadened the basis for an obviousness rejection, it did not eliminate the requirement for a ***reason*** to modify the cited references as would be required to arrive at the claimed invention. *See Takeda Chem. Industs., Ltd. v. Alphapharm Pty, Ltd.*, 492 F.3d 1356 (2007). Merely because aspects of references ***can*** be combined in order to achieve a claimed invention does not render the invention obvious.

Applicant also emphasizes that the claimed compositions achieve results that are unexpected in view of Menezo and Skrabanja. In particular, the claimed compositions are specifically designed to achieve ovulation induction without ovarian hyperstimulation. "According to the invention, the ratio of FSH to hCG in such a composition is conducive, upon administration of the composition, to folliculogenesis and to follicular maturation without ovarian hyperstimulation." Specification, paragraph [0020]; *see also* paragraph [0021]. In contrast, Menezo is specifically directed to methods for controlled ovarian hyperstimulation (COH), *see* Title. At page 2, paragraph 2, Menezo states that, "[a]s is well known and recognized in the art, techniques or methods of ovulation induction (OI) are distinct from methods of COH, although both may involve the administration of FSH." Thus, the skilled artisan would not expect from Menezo (or Skrabanja) that a composition as claimed could achieve ovulation induction without ovarian hyperstimulation.

The Supreme Court in *KSR* confirmed the significance of unexpected results to an obviousness analysis, noting that a combination that "does no more than yield ***predictable*** results" is indicative of obviousness. *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1739 (2007) (emphasis added). Where, as here, the claimed invention yields ***unpredictable*** results, the obviousness rejection is not proper under *KSR*.

At page 9, the Office Action asserts that "Applicant's arguments regarding unexpected results . . . are not found persuasive because the instant claims are drawn to a formulation . . . not to a method of inducing ovulation without ovarian hyperstimulation." Applicant respectfully reminds the Examiner that unexpected results achieved by a claimed composition can indeed overcome an obviousness rejection of composition claims. For the Examiner's convenience, Applicant provides a brief discussion of relevant case law on point.

For example, "[a] *prima facie* case of obviousness [of a chemical compound] based on structural similarity is rebuttable by proof that the claimed compounds possess unexpectedly advantageous or superior properties." MPEP § 2144.09.VII (citation omitted). In a precedential decision cited in the MPEP, the CCPA held that an increase in ***activity*** of the claimed compound as compared to a closely related prior art compound (a compound with "close structural similarity") was sufficient to overcome an obviousness rejection. MPEP § 2144.09.VII (citing *In re Weichert*, 370 F.2d 927 (CCPA 1967)). In a similar case, the CCPA held that when a claimed compound possesses an ***activity*** which a closely related prior art compound does not, an obviousness rejection is improper. *See* MPEP § 2144.09.VII (citing *In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)). In *KSR*, the Supreme Court reaffirmed that product claims could be patentable due to unexpected properties evident when the product is put to use. For example, the Court noted:

> When Adams designed his ***battery***, the prior art warned that risks were involved in using the types of electrodes he employed. The fact that ***the elements worked together in an unexpected and fruitful manner*** supported the conclusion that Adams's design ***was not obvious*** to those skilled in the art.

KSR Int'l Co. v. Teleflex, Inc., 550 U.S. 398, 416 (2007) (emphasis added).

Because the results achieved by the claimed compositions— inducing ovulation without ovarian hyperstimulation—could not have been predicted from the cited references, the obviousness rejection based on Menezo and Skrabanja should be withdrawn.

C. Claim 37 in view of Sharma and Skrabanja

At pages 12-13 of the Office Action, claim 37 is newly rejected as obvious in view of the combination of Sharma and Skrabanja. Applicant respectfully traverses.

Claim 37 depends from claim 34, which, as discussed above, is directed to a single product comprising (i) a first pharmaceutical composition comprising recombinant FSH and (ii) a second pharmaceutical composition comprising recombinant hCG, wherein the amount of recombinant hCG in the second pharmaceutical composition is selected from the group consisting of 1, 2, 3, 4 or 8 μg hCG. As shown above, Sharma does not teach a product

according to claim 34. Combining Sharma with Skrabanja does not render obvious the embodiments recited in claim 37, e.g., the product of claim 34 further comprising a syringe.

In this regard, Applicant emphasizes that neither Sharma nor Skrabanja (alone or in combination) teach or suggest a pharmaceutical composition comprising recombinant hCG in any of the specific amounts recited in claim 34 (1, 2, 3, 4 or 8 μg). Moreover, neither Sharma nor Skrabanja (alone or in combination) teach or suggest a single product comprising both (i) a recombinant FSH composition and (ii) a recombinant hCG composition. Thus, when the subject matter of claim 37 is considered as a whole, it is apparent that the combination of Sharma and Skrabanja does not make out a valid case of obviousness. Applicant therefore respectfully requests reconsideration and withdrawal of the rejection based on Sharma and Skrabanja.

VI. Obviousness-Type Double Patenting

The provisional obviousness-type double patenting rejections over co-pending applications 11/898,470 and 11/979,265 are maintained. As these applications both are still undergoing active prosecution, Applicant again respectfully defers addressing the rejections on their merits until one or more of the applications are otherwise in condition for allowance.

As noted in MPEP 804, the purpose of a provisional obviousness-type double patenting rejection is to alert the Applicant of the potential problem. The Examiner should continue to make the rejection, as appropriate, unless and until the rejection is the only issue remaining in the first-filed application, or is otherwise overcome on the merits or via a Terminal Disclaimer. Applicant therefore will take the appropriate action, if any is necessary, in due course.

CONCLUSION

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing or a credit card payment form being unsigned, providing incorrect information resulting in a rejected credit card transaction, or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date March 19, 2010 By _____

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